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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| [illegible] | [illegible] | KIM J | VPI97-101-CI |

HM22/1218

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| EXAMINER | |
|---|---|
| ALLEN, M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1631 | 10 |

**DATE MAILED:** 12/18/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/303,216 | KIM ET AL. | |
| | Examiner | Art Unit | |
| | Marianne Allen | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 1999* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

15)☐ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *91/2* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

Applicant's election of Group I, claims 1-6, in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 7-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particular HCV NS3 helicase/$dU_8$ complex crystallized in the examples and the particular crystallization methods set forth therein, does not reasonably provide enablement for all crystalline compositions and methods therefore encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is directed to producing crystals of sufficient quality so as to be suitable for structural studies by X-ray crystallography.

The prior art to at least Brown et al. (Methods in Molecular Biology, 1996) makes clear that crystallization of protein-DNA complexes is not predictable and requires guidance and extensive experimentation that would not be considered routine to develop crystals suitable for X-ray crystallography. There is no general rationale in determining the best conditions for

cocrystallizing these complexes. (See at least page 299, first full paragraph; page 300, first full paragraph; page 306, section 3.4.2; page 311, section 4 of Brown et al.) Successful purification and crystallization conditions for a particular protein/nucleic acid complex would not be expected to be predictive of the conditions required for crystallizing another complex even if it was similar. Note that the crystallization conditions for Yao et al. (Nature Structural Biology, 1997) for the helicase absent an oligonucleotide are substantially different from those of the examples.

The specification defines "HCV NS3 helicase protein" on pages 12-14 of the specification broadly and as including unrelated sequences on the N- and C-terminal ends. Also included are mutated forms with deletions, substitutions, and insertions. First of all, the specification does not clearly define the metes and bounds of those proteins included by the phrase "HCV NS3 helicase protein." Secondly, the present specification fails to provide sufficient guidance to enable one to produce the crystallizable compositions and crystallized complex encompassed by the claims such that they would be suitable for crystallization in view of the acknowledged unpredictability of producing such crystals. The specification fails to provide sufficient guidance as to those crystallization conditions or method steps that would produce crystalline compositions commensurate with the claims. As such, the specification can only be viewed as enabling the crystalline compositions specifically exemplified and those particularly exemplified methods of crystallizing them.

Applicant is advised that for purposes of enablement "crystallizable composition" and "crystallized complex" are being interpreted as suitable for producing X-ray crystallographic

quality crystals in keeping with the specification disclosure. Furthermore, limitations such as "crystallizable composition" require actually having produced a crystal from the composition as it is not so predictable that all proteins or complexes can actually be crystallized.

Claims 1-2 and 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 6 refer to an amino acid range of SEQ ID NO: 1. However, SEQ ID NO: 1 is a DNA sequence.

Claims 1 and 6 refer to crystallizable compositions; however, these claims are confusing in that these limitations appear to be circular. That is, in step (a) of the method of claim 6, how can one obtain a crystallizable composition without already having determined that it can be crystallized? Furthermore, in step (b), subjecting the composition to conditions which promote crystallization generically may or may not result in a crystallized complex.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Morgenstern et al. (Journal of Virology, 1997).

Morgenstern et al. discloses a composition which contains an HCV NS3 helicase and an oligonucleotide. (See page 3769, left column, helicase assay.) The composition is considered to meet the limitation of crystallizable in that it could be frozen which would produce crystals. Note that the claims do not require isolated components, X-ray crystallographic quality crystals, or that the composition is actually crystallized. Further note that comprising language permits inclusion of larger sequences. The RNA substrate used is larger than 12 nucleotides in length.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 9:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning the formalities of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is (703) 308-0009.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1600~~
AU1631